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Pre-CAR-T Antibiotic Exposure and Gut Microbiome Disruption as Predictors of Response and Survival in Hematologic Malignancies: A Systematic Review

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INTRODUCTION

CAR-T therapy has transformed the treatment of relapsed or refractory hematologic malignancies, but response and immune-mediated toxicity remain variable. Broad-spectrum antibiotics may disrupt the gut microbiome, alter microbial metabolites, and influence systemic immunity and CAR-T efficacy.

AIM

To evaluate associations between pre-CAR-T antibiotic exposure, gut microbiome features, and microbial metabolites with treatment response, survival, cytokine release syndrome, and neurotoxicity.

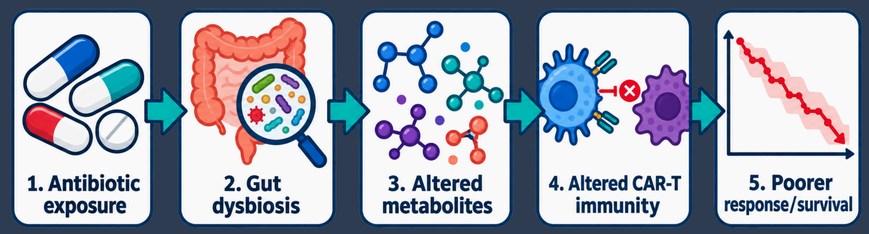
DESIGN & METHODS

This systematic review followed PRISMA guidelines. PubMed/MEDLINE, Embase, Web of Science, and the Cochrane Library were searched for studies published from 2022–2026 evaluating antibiotic exposure, gut microbiome features, or microbial metabolites in CAR-T recipients. Clinical response, survival, toxicity, and microbiome-related outcomes were extracted.

9 studies | 1,855 patients
- **6 antibiotic-exposure studies**
- **5 microbiome/metabolite studies**
- **4 integrated clinical outcomes**

Cohort	Antibiotic exposure	OUTCOME
Anti-CD19, n=228	Anaerobe-active antibiotics within 4 weeks pre-CAR-T	Worse OS
CD19/BCMA, n=329	Pre-CAR-T antibiotics	OS: 216 vs 559 days; aHR 2.52
Myeloma or lymphoma, n=334	Pre-CAR-T antibiotics	CR: 40.0% vs 57.8%; shorter PFS/OS

- Comparisons are between antibiotic-exposed and unexposed patients.



RESULTS

- Across six studies, pre-CAR-T antibiotic exposure was associated with lower response and shorter progression-free and overall survival.
- Anaerobe-active broad-spectrum antibiotics showed particularly unfavorable associations.
- Favorable response was associated with B. fragilis, B. longum, Akkermansia, Ruminococcus, Prevotella, Butyricicoccus, and inosine/short-chain fatty acid/butyrate pathways.
- Associations with cytokine release syndrome and neurotoxicity were heterogeneous.

LIMITATIONS

Study designs, antibiotic definitions, microbiome methods, and outcome reporting were heterogeneous; findings were not pooled.

CONCLUSION

Pre-CAR-T antibiotic exposure and gut microbiome disruption were consistently associated with poorer response and shorter survival.

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